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Original article

Factors influencing depression endpoints research (FINDER): Study design and population characteristics☆

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Abstract

Factors influencing outcomes of depression in clinical practice, especially health-related quality of life (HRQoL), are poorly understood. The Factors Influencing Depression Endpoints Research (FINDER) study is a European prospective, observational study designed to estimate the HRQoL of adults with a clinically diagnosed depressive episode at baseline, and 3 and 6 months after commencing antidepressant medication. We report here the study design and baseline patient characteristics.

HRQoL was assessed by the 36-item Short-Form Health Survey (SF-36) and European Quality of Life-5 Dimensions (EQ-5D). Patient ratings on Hospital Anxiety and Depression Scale (HADS) and pain Visual Analogue Scale (VAS) were also obtained. Results ($n = 3468$) showed that SF-36 mental component summary (mean 22.2) was more than two SDs below general population norms (mean 50.0) and one SD below clinical depression norms (mean 34.8); the physical component summary (mean 46.1) was similar to general population (mean 50.0) and clinical

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depression norms (mean 45.0). Mean EQ-5D scores were also lower than general population norms. Mean HADS-Depression and -Anxiety subscores were 12.3 and 13.0, respectively. Fifty-six percent of patients reported an overall pain VAS score of at least 30 mm and 70% of these patients had no physical explanation for their pain.

Further investigation into factors associated with HRQoL in depression after treatment initiation is warranted.
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Keywords: Depression; Europe; Observational study; Quality of life

1. Introduction

Depression is a common psychiatric disorder, with prevalence of major depression in Europe at around 5% [37]. The European Study of Epidemiology of Mental Disorders (ESEMeD) reported an overall annual prevalence of 3.9% for major depression and a lifetime prevalence of 12.8% [16]. Prevalence varies across European countries and between urban and rural settings [2,16].

Currently, depression is the fourth leading cause of disease burden worldwide, and it is estimated that by 2020 it will be the second [34]. The high disease burden is reflected in associated morbidity and mortality. Patients with depression have reduced functioning and impaired health-related quality of life (HRQoL) [21,25,46]. Depression is also associated with increased healthcare service utilisation and increased societal costs, such as costs due to work days lost [22,37].

Although the efficacy of antidepressant medications and psychotherapeutic treatments is well established [19], their effectiveness in improving a broad range of outcomes is less clear. The goal of treatment is to achieve remission (generally defined as no or minimal symptoms and a return to normal functioning) as this is associated with a lower risk of relapse [29]. Various factors have been reported to influence the likelihood of achieving remission, including the severity and chronicity of depression and demographic factors such as ethnicity, gender, employment, education or income [39]. Other factors are the presence or absence of anxiety symptoms, painful physical symptoms, co-morbidities and adherence to treatment [3,10,17,38,40]. It is less well understood to what extent these factors influence patient functioning and HRQoL.

Remission is assessed by prospective studies, particularly randomised controlled trials (RCTs). The generalisability of these results is often limited by the selectivity of the participating patients. As HRQoL may be affected by multiple factors, observational longitudinal studies can determine outcomes in a heterogeneous group of patients who receive treatment or intervention in routine practice. Differences in healthcare systems and access to healthcare (country, urban/rural setting or primary/specialist care) could be important factors in addition to patient characteristics in assessing outcomes.

Factors Influencing Depression Endpoints Research (FINDER) is a multinational study designed to increase the understanding of the factors that influence HRQoL outcomes for patients with a depressive episode in primary and specialist care settings. The main objective of the study is to estimate HRQoL at baseline (untreated) and at 3 and 6 months after commencing antidepressant therapy. In addition, it aims to describe the relationship between variables at baseline (including depression, anxiety, somatic and pain symptoms), and to describe the impact that baseline factors and treatment choices have on outcomes at 3 and 6 months.

The present paper reports the study design and describes the characteristics of the study population at baseline. A further paper describes the baseline prescribing patterns of initial antidepressants in the European countries participating in FINDER and the factors influencing initial antidepressant choice [7].

2. Methods

2.1. Study design

FINDER is a 6-month, observational, naturalistic, multicentre study conducted in 12 European countries: Austria, Belgium, France, Germany, Ireland, Italy, Netherlands, Norway, Portugal, Sweden, Switzerland and the UK. Patients were enrolled between May 2004 and September 2005. The study had a non-interventional design, with all treatment decisions at the discretion of the participating physician. Data were collected at baseline (the routine visit at which the patient agreed to enter the study) and at 3 and 6 months post-baseline during visits that were part of routine clinical care.

The study was approved in all countries according to local requirements for ethics and/or regulatory approvals for observational studies. Subsequent to clinical diagnosis and the decision to treat with an antidepressant, patients gave written informed consent for the provision and collection of data during the observation period.

2.1.1. Patients

Patients were eligible for inclusion if they presented within the normal course of care and (1) were clinically diagnosed by their physician as suffering from depression, (2) were about to start antidepressant pharmacological treatment for either a first or subsequent episode of depression (the index episode), (3) were aged at least 18 years, and (4) were not simultaneously participating in another study that involved an investigational drug or procedure.

2.1.2. Investigators

Participating investigators were primary care physicians (PCPs) or specialists. Across the 12 participating European countries, eligible patients were enrolled by 437 investigators

(211 PCPs [48.3%], and 226 psychiatrists, neurologists and other specialities [51.7%]). Although type and proportion of investigators varied by country (Fig. 1), it most often reflected country-specific variations in healthcare delivery. Demographic data on age and gender of investigators were collected. FINDER included investigators from rural (62.7%) and urban (27.3%) locations as well as public and private facilities.

2.2. Data collection and assessments

Data were collected on local language forms at baseline, and at 3 and 6 months (±1 month) post-baseline. Any patients not making a routine visit to their physician within the defined data collection interval were retained in the study and could have data collected the next time they presented within a data collection interval.

2.2.1. Patient characteristics

At baseline, data on socio-demographics, psychiatric history and the occurrence of psychiatric disorders in the previous 24 months were prospectively collected by the physician based on patient interviews. The presence of specified co-morbid chronic physical conditions and functional syndromes in the previous 24 months was recorded, as was whether or not the patient had suffered any physical trauma in the previous 24 months, or whether they had presented with physical symptoms in the previous 24 months for which a cause could not be identified.

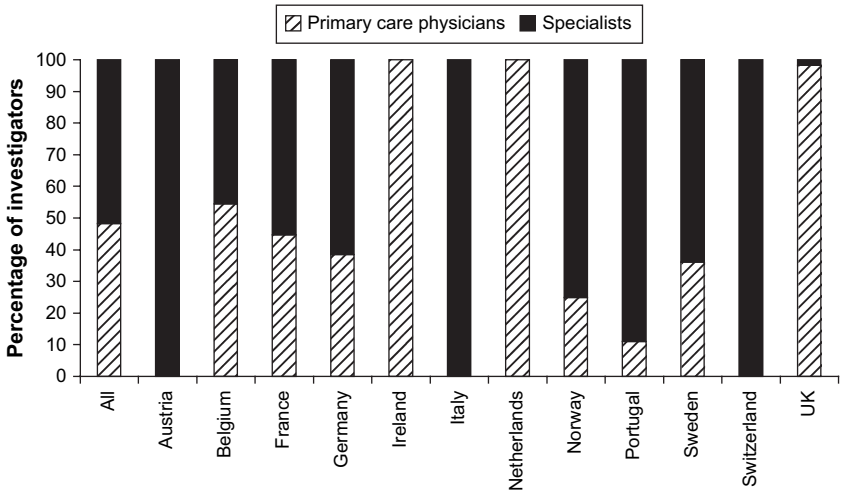
Healthcare resource utilisation and psychotherapy in the previous 24 months were recorded as well as use over the 3 and 6 month follow-up periods (psychotherapy data were not collected in the UK). For the same periods, data regarding the intake of antidepressants and analgesics (both over-the-counter and prescribed) were also collected. Antidepressant type, mean daily dose, start and stop date, and reason for discontinuation were recorded. Information on other prescribed concomitant medications (mood stabilisers, anxiolytics/hypnotics and antipsychotics) taken at the time of entry into the study and since study entry was collected at the 3 month (all countries except the UK) and 6 month (all countries) visits.

2.2.2. Health-related quality of life (HRQoL) assessment

HRQoL was assessed at baseline, and 3 and 6 months using the 36-item Short-Form Health Survey (SF-36) version 2 [45] and the European Quality of Life-5 Dimensions (EQ-5D) questionnaire [11].

The SF-36 is a widely used, self-administered, generic instrument for measuring HRQoL. Thirty-six questions generate scores across eight health domains (subscales) and two summary scores: the physical component score (PCS) and the mental component score (MCS). Norm-based scoring was used for all eight SF-36 domains, with a mean of 50 and a standard deviation (SD) of 10 based on general US population data, as European norms for all participating countries are unavailable at present but US norms correlate highly with existing country-specific measures and are recommended to be used in multinational studies [44]. Norms for clinical depression were available for PCS (mean 45.0 [SD 12.1]) and MCS (mean 34.8 [SD 12.2]). Higher scores indicate better HRQoL.

The EQ-5D is a validated instrument for measuring health outcomes consisting of two parts [11]: (1) a Visual Analogue Scale (VAS) assessing overall health on the day scoring from 0 (worst imaginable health state) to 100 (best imaginable health state); and (2) five questions covering mobility, self-care, usual activities, pain/discomfort and anxiety/depression, each scored on a 3-point scale (1 = no problems, 2 = some/moderate problems, and 3 = extreme problems). For each



	All	Austria	Belgium	France	Germany	Ireland	Italy	Netherlands	Norway	Portugal	Sweden	Switzerland	UK
No.investigators	437	18	33	103	65	10	38	39	8	9	36	20	58
No. patients enrolled	3515	164	240	612	674	68	514	199	40	53	204	139	608
No. patients eligible	3468	163	239	606	649	68	513	196	40	48	199	139	608

Fig. 1. Investigators (%) who enrolled eligible patients by country.

patient with complete data, responses to the five questions were converted to a single Health State Index (HSI) on a scale ranging from 0 to 1, with a higher score indicating better HRQoL [15]. For both SF-36 and EQ-5D, official language versions were available for all participating countries.

2.2.3. Depression assessment

The patient-rated Hospital Anxiety and Depression Scale (HADS) [48] was completed at baseline and 3 and 6 months. The HADS consists of seven items each for depression (HADS-D) and anxiety (HADS-A) scored on a 4-point scale from 0 to 3. For both subscales, a score of $\geq$11 indicates 'probable case' (i.e. probable presence of the mood disorder), 8–10 indicates 'doubtful case' and $\leq$7 indicates 'non-case' [48]. For analysis, all items within each HADS subscale had to be answered otherwise the subscale was set to missing. As published normative data for the HADS are limited, values obtained from a general UK adult population were used for reference purposes [14].

2.2.4. Somatic and pain assessment

Painful symptoms were evaluated at baseline, and 3 and 6 months using the 28-item Somatic Symptom Inventory (SSI-28) [6] and six VAS [9] with the aim of exploring possible relationships between depression, HRQoL and pain.

The SSI-28 consists of seven pain-related items and 21 items not relating to pain. Patients rated the degree to which each symptom bothered them over the past week on a scale of 1 (not at all) to 5 (a great deal).

Overall pain severity was rated by patients using a horizontal VAS marked 'no pain' at one end (0 mm) and 'as severe as I can imagine' at the other end (100 mm), as were each of the following: headaches, back pain, shoulder pain, interference with daily activities and time in pain while awake. Patients with an overall pain VAS score of 30 mm or more were defined as having 'moderate/severe pain' [13,30]. This threshold score together with the presence of chronic conditions was used to stratify patients into three groups: (1) no/mild pain; (2) moderate/severe pain with a defined co-morbid chronic physical condition and/or co-morbid functional syndrome present known to cause pain, termed 'medically explained pain'; and (3) moderate/severe pain with a defined co-morbid physical condition and/or co-morbid functional syndrome present but not associated with pain, or those without further co-morbidity, termed 'medically unexplained pain'. Pain in the study population was further characterised by analysing the SF-36 bodily pain domain and the EQ-5D pain/discomfort item.

2.3. Statistical analysis

Descriptive summary statistics (means, standard deviations [SDs], frequencies, percentages) were used to describe the baseline characteristics of the study population. Longitudinal data from the FINDER study will be presented in a follow-up publication.

Patients were excluded from the analysis if one or more entry criteria were violated or from individual analyses based on missing, implausible (according to pre-defined ranges) or uninterpretable data. The exclusion of patients' data from analysis was based on study entry criteria at the first observation, not on whether or not antidepressant medication was taken during the 6 month follow-up period. Only 47 patients were excluded from the analysis (1.3%) due to failure to meet any of the entry criteria. Data were analysed using SAS version 8.2.

3. Results

In total, 3515 patients were enrolled and data from 3468 (98.7%) were eligible for analysis. Most patients were enrolled in Germany, France, UK and Italy, with fewer than 100 patients each from Ireland, Portugal and Norway (Fig. 1).

3.1. Patient characteristics and psychiatric and medical histories

Patients' socio-demographic characteristics are presented in Table 1.

Regarding psychiatric history, patients had a mean duration of depressive illness of 8.5 years (SD 10.4) and 45.1% had a history of at least one other depressive episode in the previous 2 years (excluding the index episode) (Table 2). Anxiety disorder and/or panic disorder in the previous 2 years were also common (51.1%).

The mean duration of the current episode of depression was 13.6 weeks (SD 16.5). For patients who had previous episodes of depression, the mean time between remission of the previous episode and onset of the index episode was 24.8 weeks (SD 20.1).

A large proportion of patients had at least one co-morbid chronic physical condition (42.5%) or co-morbid functional syndrome (39.9%) at study entry (Table 3). Hypertension was the most common co-morbid chronic physical condition (20.0%) and chronic fatigue syndrome was the most common co-morbid functional syndrome (25.3%).

Table 1
Baseline socio-demographic characteristics of the study patient population

	Patients
Enrolled patients (*N*)	3515
Patients eligible for analysis (*N*)	3468
Mean (SD) age [range] (years)	46.8 (14.7) [18–93]
Gender female/male (%)	68.2/31.8
No or mandatory level of education[a] (%)	52.3
Cohabiting[b] (%)	58.6
Unemployed (%)	13.7
In paid work (%)	50.1
Mean (SD) number of dependants	1.1 (1.3)
Mean (SD) BMI (kg/m^2)	25.5 (5.2)
Current smoker (%)	32.3

BMI: Body Mass Index; SD: standard deviation.
[a] Reference is further, university or post-graduate education.
[b] Includes married or domestic partner vs. divorced, legally separated, widowed, partner living separate or no relationship.

Table 2
Psychiatric history of patients at the baseline visit

	Patients
Previous depression episodes	
Mean (SD) duration of depressive illness [range] (years)	8.5 (10.4) [0–71]
Mean (SD) age at first episode [range] (years)	38.4 (14.7) [14–91]
Percentage of patients who had at least one other depressive episode in previous 2 years (excluding index episode)	45.1
Mean (SD) number of depressive episodes in previous 2 years (excluding index episode) [range][a]	1.8 (1.4) [1–20]
Mean (SD) duration of the depressive episode (weeks) preceding index episode [range][a]	17.1 (14.5) [1–96]
Current (index) episode of depression	
Mean (SD) duration [range] (weeks)	13.6 (16.5) [1–104]
Mean (SD) time between previous episode's remission and onset of index episode [range] (weeks)[a]	24.8 (20.1) [1–98]
Other psychiatric disorders in previous 2 years[b]	
Anxiety disorder and/or panic disorder (%)	51.1
Obsessive compulsive disorder (%)	9.0
Drug and/or alcohol dependence disorder (%)	6.9

SD: standard deviation.
[a] Only for patients who had a previous episode of depression within 2 years.
[b] Reported if >5%. Others from selected list were bipolar disorder and schizophrenia.

Table 3
Co-morbid chronic physical conditions and functional syndromes at the baseline visit

	Patients
Patients with at least one co-morbid chronic physical condition[a] (%)	42.5
Mean (SD) number of co-morbid chronic physical conditions[a]	0.7 (1.1)
Patients with different types of co-morbid chronic physical conditions[b] (%)	
Hypertension	20.0
Rheumatological disorder	10.9
Asthma	6.7
Diabetes	5.7
Other (than neuropathic) neurological disorder	5.3
Patients with at least one co-morbid functional syndrome[c] (%)	39.9
Mean (SD) number of co-morbid functional syndromes[c]	0.7 (1.1)
Patients with different types of functional syndromes[d] (%)	
Chronic fatigue syndrome	25.3
Irritable bowel syndrome	16.1
Atypical chest pain	11.1
Irritable bladder	7.4
Fibromyalgia	7.0

SD: standard deviation.
[a] Listed conditions were diabetes, angina, hypertension, asthma, malignant disease, neuropathic disorder, other neurological disorder, rheumatologic disorder, other chronic condition.
[b] Reported in table if >5%. Angina, neuropathic disorder and malignant disease were present in 3.7%, 2.7% and 2.5% of patients, respectively. Other chronic conditions were present in 14.3% of all patients.
[c] Listed conditions were irritable bowel syndrome, chronic fatigue syndrome, atypical chest pain, irritable bladder, fibromyalgia, chronic pelvic pain.
[d] Reported in table if >5%. Chronic pelvic pain was present in 4.9% of patients.

3.2. Baseline scores

Fig. 2 shows SF-36 scores with the mean MCS (22.2, SD 10.0) and mean PCS (46.1, SD 10.3) plotted together with general population and clinical depression norms.

The mean scores of the EQ-5D HSI and VAS for the study population (Table 4) were just over half of those of European population norms. Problems were most often recorded in the anxiety/depression, pain/discomfort and usual activities dimensions of the EQ-5D. Almost three-quarters (73.3%) of patients had moderate or extreme pain/discomfort on the EQ-5D pain/discomfort domain (Table 5).

The mean HADS-D score (12.3, SD 4.5) of the study population was much higher than that of the UK general adult population (3.7, SD 3.1) [14] (Table 4). On the basis of HADS-D cut-offs, 66.3% of all patients were considered to be probable cases of depression, 18.5% were doubtful cases and 15.2% were non-cases. The patients also had a higher mean HADS-A score (13.0, SD 4.0) than the UK general adult population (6.1, SD 3.8). Of the patients in this study, 74.1% were probable cases of anxiety, 16.6% were doubtful cases and 9.3% were non-cases for anxiety.

The mean overall pain VAS score was 39.6 (SD 28.8). Mean scores for all VAS pain scales are summarised in Table 5. Pain interfered with work at least moderately in 55.1% of patients (SF-36 single item). Of the different locations of pain symptoms (SSI-28), headaches were the most common (Table 5).

3.3. Relationship between depression, HRQoL and pain at baseline

With respect to the three pain groups, 1447 patients (43.7%) had no/mild pain, 1311 (39.6%) had medically unexplained moderate/severe pain and 550 (16.6%) had medically explained moderate/severe pain. In the first group, mean scores on the SF-36 bodily pain domain and PCS were at least one SD higher than in patients with medically explained pain or medically unexplained pain (Fig. 3).

The mean HADS-D score at baseline was higher in patients with six or seven pain-related items on the SSI-28 than in those with fewer pain symptoms (Fig. 4). The mean HADS-D score also increased with increasing pain severity on the EQ-5D pain/discomfort dimension: no pain/discomfort, 11.4 (SD 4.6); moderate, 12.3 (SD 4.3); and extreme, 14.4 (SD 4.2).

4. Discussion

There is increasing debate in the healthcare literature about the 'efficacy gap' and assessment of the 'relative effectiveness' of healthcare interventions, especially for publicly funded healthcare systems where demand always exceeds available resources [20] and where physicians and decision-makers must choose between different treatments [28]. By providing further information about the management of depressed patients in real life settings, observational studies complement RCT

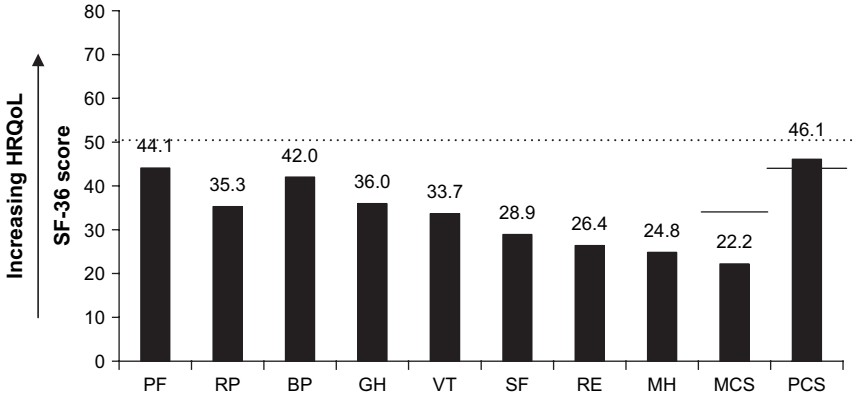


Fig. 2. Mean SF-36 domain scores and mental and physical health component summary scores (all norm-based) for the study population at baseline. Dotted line represents the general population norm (mean 50). Solid lines represent clinical depression norms (PCS mean 45.0; MCS mean 34.8). A higher score indicates better quality of life. PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health; MCS, mental component score; PCS, physical component score.

findings and provide information about the benefits of different treatments on patient outcomes [31]. FINDER was designed to provide further information and increase the understanding of the factors that influence HRQoL outcomes for patients receiving antidepressant medication for a depressive episode in routine primary and specialist care settings. A few study design characteristics are of note: (1) the setting in primary and secondary care; (2) criteria for patient inclusion; and (3) longitudinal design. The second objective of this paper, the characteristics of the FINDER study population, will also be discussed.

4.1. Primary and secondary care settings

FINDER, unlike other large European observational studies [2,8,16,33,42], includes patients in primary and specialist care. Most episodes of depression and anxiety are managed in primary care, with cross-sectional studies highlighting that fewer than half of these episodes are identified during consultation largely because of somatic presentation by patients [43]. Many primary care patients present with a combination of physical, somatic and painful symptoms rather than the classic emotional symptoms of depression [18]. Further exploration of the FINDER data set will

Table 4
EQ-5D and HADS scores at baseline for the total patient population

	Study population	General population
EQ-5D		European countries ($N = 21{,}004$)[a]
Health State Index score (0–1)	0.44 (0.31)	0.85 (0.23)
VAS score (0–100)	44.8 (20.4)	77 (20)
Dimensions, % with any problem		
Anxiety/depression	96.6	24.7
Pain/discomfort	73.3	37.9
Usual activities	72.5	14.6
Mobility	33.8	17.1
Self-care	18.3	4.9
HADS		UK adults ($N = 1792$)[b]
HADS-D	12.3 (4.5)	3.7 (3.1)
HADS-A	13.0 (4.0)	6.1 (3.8)

All data are presented as mean (SD) unless indicated otherwise. EQ-5D: European Quality of Life-5 Dimensions questionnaire; SD: standard deviation; VAS: Visual Analogue Scale; HADS-D: Hospital Anxiety and Depression Scale-Depression subscale; HADS-A: Hospital Anxiety and Depression Scale-Anxiety subscale.

[a] From Szende and Williams [41].

[b] From Crawford et al. [14].

Table 5
Pain assessment at baseline

Measure	Patients *N* (%)
Pain severity, EQ-5D pain/discomfort domain	
None	918 (26.7)
Moderate	2100 (61.2)
Extreme	414 (12.1)
Pain interference with normal work, SF-36 single item	
Not at all	818 (23.8)
A little bit	725 (21.1)
Moderately	872 (25.4)
Quite a bit	745 (21.7)
Extremely	275 (8.0)
Pain symptom location, SSI-28 pain-related items, patients bothered moderately/quite a bit/a great deal	
Headaches	1676 (49.0)
Soreness in muscles	1561 (46.0)
Pain in lower back	1557 (45.8)
Neck pain	1536 (44.9)
Pain in joints	1469 (43.1)
Pain/cramps in abdomen	1019 (30.1)
Pain in heart/chest	955 (26.3)
VAS scores for pain,[a] mean (SD)	
Overall pain	39.6 (28.8)
Severity of headaches	30.5 (29.5)
Severity of back pain	32.2 (30.7)
Severity of shoulder pain	24.7 (29.8)
Interference of overall pain with ability to perform daily activities	39.2 (31.6)
Amount of time had pain while awake	42.0 (32.5)

Data presented as *N* (%) of patients unless indicated otherwise.

[a] During past week; VAS score 0–100.

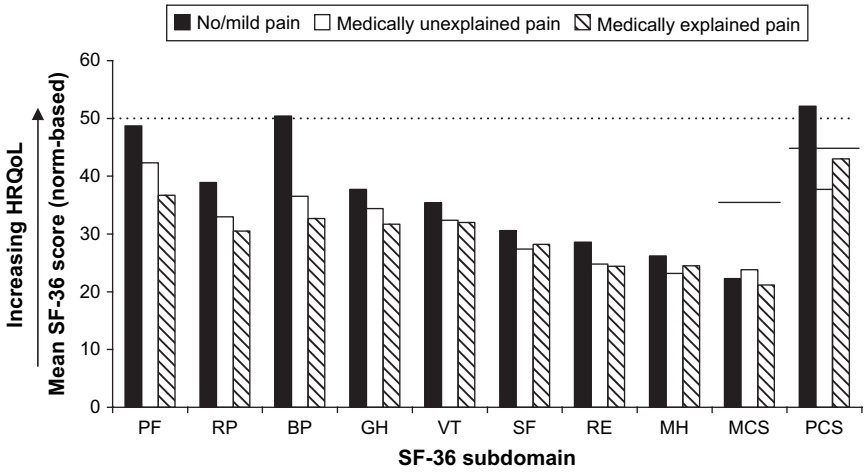


Fig. 3. SF-36 scores by pain group. Dotted line represents the general population norm (mean 50). Solid lines represent clinical depression norms (PCS mean 45.0; MCS mean 34.8). A higher score indicates better quality of life. PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health; MCS, mental component score; PCS, physical component score. Patients with no/mild pain had an overall VAS score <30 mm whereas patients with medically explained or unexplained pain had moderate/severe pain defined as an overall VAS pain score ≥ 30 mm.

allow us to examine the influence of primary and secondary care settings in treatment outcomes.

4.2. Criteria for patient inclusion

Almost half of the investigators in FINDER were PCPs and therefore unlikely to administer psychiatric procedures to diagnose depression. Consistent with the observational nature of the study, patient eligibility for study entry relied on a clinical diagnosis of depression. In addition, patients completed the HADS, which has excellent psychometric properties in specialist and primary care populations [35,36]. According to the subscale scores, 66% and 72% of patients had 'probable caseness' of depression and anxiety, respectively, demonstrating that a clinical diagnosis of depression in a naturalistic study may deviate from instrument-based diagnosis.

4.3. Longitudinal design

The analysis described here is cross-sectional for patients enrolled in the FINDER study and as such highlights the important relationship between depression, quality of life and pain. The longitudinal design of the study will enable us to observe HRQoL improvements during treatment in everyday clinical practice, as well as to increase the understanding of factors associated with those outcomes in further analysis.

4.4. FINDER baseline results

HRQoL outcomes provide a broader view of the patient's overall well-being, compared with traditional depression rating scales. In some countries, like the UK, clinicians have called to have HRQoL outcomes measured along with more conventional outcome measures [1]. It is argued that patients and clinicians differ in their assessment of the severity of illness and effects of treatment but the patient is the only valid source of HRQoL information. HRQoL data in depression are limited. Some consider HRQoL as a measure of impairment, disability and handicap (in symptoms and function) that can be labelled as ''health status''. Others argue that this is too restrictive and a ''needs based'' approach should

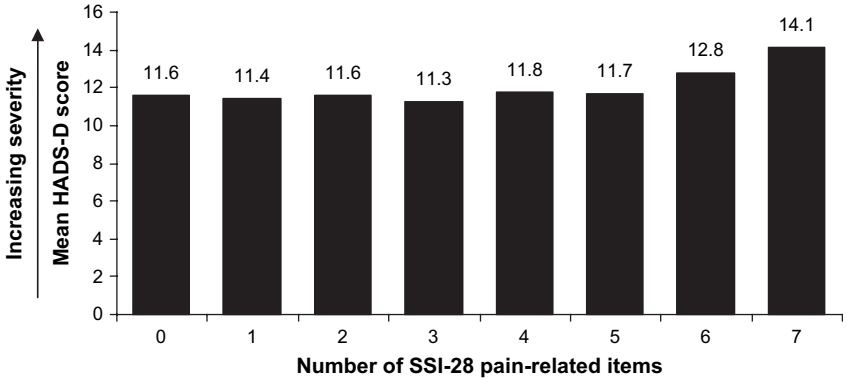


Fig. 4. Depression score (mean HADS-D) according to number of pain-related items present on SSI-28. HADS-D: hospital anxiety and depression scale- depression subscale; SSI-28: somatic symptom inventory-28.

be used [47]. In FINDER we refer HRQoL as a ''health status'', measuring the level of impairment and physical and social disabilities in depressed patients.

HRQoL for patients entering FINDER was lower than population norms. In particular, the mean SF-36 MCS score was more than two SDs below the population norm and about one SD lower than the norm for clinical depression, whereas the mean baseline PCS score was similar to norms. As expected for depressed patients, FINDER participants were more impaired mentally than physically.

In patients with major depression studied in primary care, those with higher depressive symptom scores had worse functional status and HRQoL [17,27]. Factors such as clinical history, medical and psychiatric co-morbidity and characteristics of the index depressive episode [39] have been reported to affect the prognosis of depression. Though the majority of these studies have been undertaken in specialist clinic samples, PCP studies are also consistent with this observation [17]. The FINDER population had considerable past psychiatric history, with 45.1% of patients reporting at least one episode of depression in the previous 2 years. The inclusion of recurrent and first episode patients will enable us to investigate further whether differences exist in their HRQoL outcomes.

Other factors relevant to HRQoL in depression, including anxiety, somatic and painful physical symptoms, have received less investigation. Indeed, many studies evaluating the association between depression and pain have assessed the emotional and psychological impacts of underlying medical disorders (i.e. secondary depression). However, pain is a common symptom associated with depression, and the presence of pain can complicate its diagnosis and treatment [5,32]. In FINDER, 56.3% of depressed patients had moderate/severe pain, whether medically explained or unexplained at baseline.

Nevertheless, the interesting question is to what extent painful symptoms affect HRQoL outcomes in depression? In this cross-sectional analysis of FINDER baseline data, we found that pain interfered with normal work in over half of the patients. Moreover, increasing pain severity and a higher number of pain-related symptoms were associated with more severe depression, although causation cannot be inferred from these data. Data from previous studies indicate that more severe pain predicts poorer depression and HRQoL outcomes [4], and further research is needed to explore the links between depression, HRQoL and pain.

4.5. Study limitations

Several limitations should be considered when interpreting the results of FINDER: (1) the sample was limited to patients initiating antidepressant treatment, thus excluding those with unrecognised depression, those untreated and those exclusively receiving a non-pharmacological treatment; (2) data collected retrospectively for the previous 2 years before study entry may be affected by recall bias; (3) the pre-specified lists of psychiatric, physical and functional conditions may not be comprehensive enough to capture all co-morbid conditions present; (4) the pre-specified list may have also prompted physicians to record certain disorders that may not withstand further diagnostic confirmation; (5) HRQoL instruments used in the study (e.g. SF-36 and EQ-5D) partly measure concepts that are also contained in depression instruments.

In addition, it is also worth noting that HADS was initially designed as a screening tool for depression. However, it has been used for the evaluation of depression, and a review of data has shown that it is sensitive to changes during the course of disease and in response to psychotherapeutic and psychopharmacological interventions [26]. Lastly, observational studies are in general accompanied by a number of potential weaknesses, such as selection bias, observer bias and confounding, mainly resulting from the absence of randomisation [23,24], e.g. it is possible that physicians participating in the study had a particular interest in psychiatry and were therefore not representative of the general PCP population. As the extent of the bias due to non-observed covariates is usually unknown, statistical techniques are limited in their ability to fully correct for those. However, the merits of an observational study lay in being complementary evidence to those derived from RCTs [12].

In conclusion, with over 3500 patients, this is the largest prospective observational study of depression and HRQoL to date. HRQoL of patients at enrolment demonstrates a substantial impairment and indicates an association between depression, HRQoL and pain. Further analysis of data from the FINDER study will provide important advances in our understanding of the factors influencing HRQoL outcomes in depression in everyday clinical practice.

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